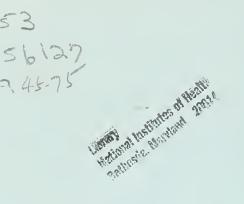


<u>H</u>IGHLIGHTS IN THE HISTORY AND ORGANIZATION OF THE NATIONAL INSTITUTES OF HEALTH 1945-1975



U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE Public Health Service National Institutes of Health



INTRODUCTORY NOTE

This chronology lists some milestones in the 30 year history of the National Institutes of Health, 1945-1975.

The material presented is of three types:

First, a chronology of principal legislative and organizational actions affecting NIH.

Second, a summary of ways in which the National Institutes of Health has broadened the national base of biomedical research, education and communication.

Finally, there is a list of specific scientific advances and discoveries resulting from research conducted or supported by the National Institutes of Health. Because it obviously is not possible to assign a specific date for progress that was attained over a long period or as a result of contributions from many sources, few dates are given.

Director of Information

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Chronology of Legislative and Organizational Actions

PRIOR TO 1945 - The National Institutes of Health had its origins in 1887 when a research laboratory was founded at the Marine Hospital, Staten Island, N.Y., to meet new responsibilities of the Marine Hospital Service. In 1891 this was renamed the Hygienic Laboratory and moved to Washington, D.C. In 1902, an Advisory Board was established for the Laboratory; this was later to become the National Advisory Health Council. In the same year, Congress gave the Service responsibility for control of biologics. In 1912 the name of the Public Health and Marine Hospital Service was changed to Public Health Service. In 1930, the Hygienic Laboratory was renamed the National Institute of Health. In 1937 Congress authorized the National Cancer Institute and the first research grants were In 1938 the National Institute of Health moved made. to Bethesda, Md. In this same year the National Cancer Institute awarded the first research fellowships. In 1944, the Public Health Service Act consolidated and revised existing public health legislation, and gave NIH general legislative authority to conduct research.

- 1946 A Research Grants Office was created at the National Institute of Health to administer the Office of Scientific Research and Development projects transferred to the Public Health Service at the end of World War II, and to operate a program of research grants and fellowship awards.
- 1947 The Division of Research Grants was established to process NIH grants and fellowships to non-Federal institutions and scientists. The first training grants were awarded.
- 1948 The National Heart Act authorized the National Heart Institute and changed the name of the National Institute of Health to National Institutes of Health. The National Heart Institute was established.
 - The National Dental Research Act authorized the National Institute of Dental Research.
 - The National Microbiological Institute and the Experimental Biology and Medicine Institute were established.
 The Rocky Mountain Laboratory and Biologics Control
 Laboratory became two of the four components of the
 National Microbiological Institute.
- 1949 The National Institute of Mental Health was established.

- 1950 The Omnibus Medical Research Act authorized the National Institute of Neurological Diseases and Blindness and the National Institute of Arthritis and Metabolic Diseases, the latter absorbing the Experimental Biology and Medicine Institute. The Act also gave the Surgeon General authority to establish new institutes. The National Institute of Neurological Diseases and Blindness and the National Institute of Arthritis and Metabolic Diseases were established.
- 1953 The Clinical Center opened, thus extending the clinical dimension of NIH research. The Clinical Center, providing twice as much laboratory space as patient-care space, and laboratories in corridors adjacent to hospital rooms, became the prototype for many other research hospitals.
 - The Public Health Service became a part of the new Department of Health, Education, and Welfare.
- 1955 The biologics control function was placed in the newly formed Division of Biologics Standards.
 - The National Microbiological Institute became the National Institute of Allergy and Infectious Diseases.
- 1956 The Health Research Facilities Act, establishing a program of matching grants for research construction in non-Federal institutions, was enacted.

- 1958 The Division of General Medical Sciences was established, extending medical research into diseases not being investigated by other NIH components.
- 1960 The Public Health Service Act was amended to provide for general support of research and research training programs in nonprofit institutions. The International Health Research Act was adopted; NIH extended its international programs.
- 1962 The National Institute of Child Health and Human Development was authorized and the Division of General Medical Sciences was redesignated the National Institute of General Medical Sciences.
 - The Division of Research Facilities and Resources was created. The National Library of Medicine, a part of the Public Health Service since 1956, moved to the NIH reservation.
- 1964 The Division of Computer Research and Technology was established.
- 1965 The Heart Disease, Cancer and Stroke Amendments of 1965 authorized regional medical programs to combat three "killer" diseases. The Division of Regional Medical Programs was established the following year to administer grants under these amendments.
- 1966 The Division of Environmental Health Sciences was established.

- 1967 The National Institute of Mental Health was separated from NIH and became a bureau of the Public Health Service. NIMH's Intramural Research Program, comprising activities conducted in the NIH Clinical Center and other NIH facilities, continued at NIH.
- 1968 Under a reorganization of health activities, NIH became an operating agency within HEW; the Bureau of Health Manpower, later renamed the Bureau of Health Professions Education and Manpower Training, and the National Library of Medicine became components of NIH.
 - The Division of Regional Medical Programs was transferred to the Health Services and Mental Health Administration.
 - The John E. Fogarty International Center for Advanced Study in the Health Sciences was established.
 - The National Eye Institute was created to build an enlarged program based on blindness research formerly conducted by the National Institute of Neurological Diseases and Blindness. The National Institute of Neurological Diseases and Blindness became the National Institute of Neurological Diseases and Stroke.
 - The Lister Hill National Center for Biomedical Communications was established at the National Library of Medicine.
 - The National Center for Population Research was established in the National Institute of Child Health and Human Development.

- 1969 The Division of Environmental Health Sciences became the National Institute of Environmental Health Sciences.
 - The Secretary of HEW redesignated the National Heart Institute as the National Heart and Lung Institute, reflecting expansion of its functions.
- 1970 Amendments of the PHS Act authorized mission-related clinical training by the National Institute of General Medical Sciences.
 - The Health Training Improvement Act of 1970 extended and amended allied health professions training and established eligibility of new Health Professions Educational Assistance Schools for "start-up" grants.
- 1971 The National Cancer Act of 1971 authorized a National Cancer Program, enlarged the authority of the National Cancer Institute, and established a National Cancer Advisory Board.
- 1972 The Division of Biologics Standards was transferred from NIH to the Food and Drug Administration where it became the Bureau of Biologics.
 - A National Sickle Cell Anemia Control Act established a national program for the diagnosis and treatment of, and counseling and research in, sickle cell disease.

- The National Institute of Arthritis and Metabolic
 Diseases was renamed the National Institute of Arthritis,
 Metabolism, and Digestive Diseases as part of a new
 emphasis on support of research and training in digestive
 diseases.
- The National Heart, Blood Vessel, Lung and Blood Act expanded the authorities of the National Heart and Lung Institute to intensify the national effort against heart, lung and blood diseases.
- The National Cooley's Anemia Control Act authorized additional funds for research on Cooley's anemia.
- The National Commission on Multiple Sclerosis Act established a Commission charged with determining the most productive avenue of researching causes and cures of this disease.
- 1973 The Bureau of Health Manpower Education was transferred from NIH to the new Health Resources Administration. The Bureau was renamed the Bureau of Health Resources Development.
- 1974 The National Cancer Act Amendments of 1974 permitted NCI to designate additional Comprehensive Cancer Centers; required peer review of grant applications and contract projects; and called for a more effective worldwide dissemination of cancer knowledge. The 1974 Amendments also established the President's Biomedical Research Panel to review research programs conducted by NIH and

by the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) and to recommend policy regarding their operation.

- The National Research Act of 1974 established a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. It also consolidated all research training authorities of NIH and ADAMHA into a unified National Research Service Awards Authority
- The Research on Aging Act authorized establishment of an eleventh Institute at NIH, the National Institute on Aging.
- The National Diabetes Mellitus Research and Education Act established a National Commission on Diabetes to formulate a long-range plan for diabetes research; directed the establishment and expansion of diabetes research and training centers; and directed establishment of a committee to coordinate research activities of the NIH, as well as activities of other Federal agencies relating to diabetes.
- The Sudden Infant Death Syndrome Act authorized the National Institute of Child Health and Human Development to carry out sudden infant death syndrome research, required Congressional reporting by the Institute, and provided for an information and counseling program.
- 1975 The National Arthritis Act of 1974 established a National Commission on Arthritis and Related Musculoskeletal diseases to formulate a long-range plan to combat arthritis through research, training, services and data systems. It

also established an Associate Director for Arthritis in the NIAMDD and a HEW Intradepartmental Arthritis Coordinating Committee and an Arthritis Screening and Detection Data Bank. It provided three-year authorizations for arthritis screening, detection, prevention and referral projects and for arthritis research and demonstration centers.

 The National Institute of Neurological Diseases and Stroke was renamed the National Institute of Neurological and Communicative Disorders and Stroke. ,

Contributions

to a

Broadened National Scientific Effort

Over the years, the single most important contribution of the National Institutes of Health may have been its comprehensive broadening of the national biomedical research base. While individual events are not easily identified in this context, some summarization is possible to provide a measure of the NIH investment in American science.

These specific gains can be cited:

175,000 non-Federal biomedical scientists have been supported by 253,000 research grants. Among these were 58 recipients of the Nobel Prize in Physiology or Medicine; three of these were NIH scientists and another one is a former NIH intramural scientist recognized for work begun at NIH and subsequently supported by the NIH at a non-Federal institution.

- More than 55,000 individual scientists have been supported in their professional development in basic science or clinical specialties by funds distributed to academic and research institutions for advanced training.
- More than 10,000 different institutions have received support for research and training programs.

- 18 million square feet of space have been added to the nation's biomedical research plant.
- Principal medical institutions in all parts of the nation established, with NIH support, 84 General Clinical Research Centers with 827 beds in which research knowledge is extended and applied expeditiously to care of patients.
- Under the Medical Library Assistance Act of 1965, health science libraries expanded their services and established 11 regional medical libraries.
- The computer-based MEDLARS (Medical Literature Analysis and Retrieval System) was pioneered and developed in the early 1960's, giving health professionals everywhere quick access to the world's biomedical literature.

Significant Research Accomplishments Conducted or Supported by the National Institutes of Health 1945-75

Developed or participated in the development of more than 40 drugs useful in the treatment of advanced cancer.

Developed an effective, frequently curative, chemotherapeutic regimen for choriocarcinoma, a rare but once fatal tumor which arises from the placenta.

Identified approximately 50 environmental agents associated with increased cancer in persons exposed, including certain metals, ores, air pollutants, and oils. This resulted in reduction of levels of exposure to many of these agents.

Identified many of the more than 100 viruses known to cause cancer in experimental animals, and investigated vaccines for prevention of some of these virus-caused cancers in animals.

Demonstrated that animal tumors can be produced by the nucleic acid core of a tumor-causing virus, and that viral genetic material is incorporated into the cellular genetic material of animals with virus-induced cancer.

Discovered an association of type-C RNA viruses with human acute leukemias, lymphomas and cancers of the connective tissue (sarcomas).

Investigated the association of herpes-type DNA viruses with Burkitt's lymphoma, cancer of the postnasal space and cancer of the uterine cervix.

Extended life for children with acute leukemia to almost 3 years after diagnosis, contrasted with the 2- to 3-month survival common in 1945, thanks to new forms of combination therapy and supportive care.

Developed the technique of platelet transfusions to prevent fatal hemorrhage in patients with acute leukemia receiving cytotoxic therapy.

Developed supportive techniques, including relatively "germfree" environments and transfusions of white blood cells, to prevent fatal infections among patients with acute leukemia undergoing myelosuppressive therapy.

Achieved a cure of 90 percent of patients with early-stage Hodgkin's disease through high-dose, intensive radiotherapy to affected lymph nodes and adjacent lymph node regions.

Achieved freedom from all evidence of advanced-stage Hodgkin's disease for 5 years for 75 percent of patients in a group treated with a combination of 4 anti-cancer drugs.

Achieved a rise to 40 percent in the proportion of women cured of early breast cancer, thanks to application of new methods for early detection and prompt, aggressive treatment.

Constructed a highly useful "coronary profile" by which physicians can identify highly susceptible individuals long before the disease produces clinical signs, and initiate preventive measures.

Applied repetitive electrical stimuli successfully in man in the first of a family of heart pacemaker devices whose development has progressed through portable battery-powered pacemakers, including completely implantable versions, to the still experimental nuclear-powered pacer currently undergoing tests in animals.

Reported the first successful use of an artificial valve in the human circulatory system. By demonstrating the feasibility of such a prosthesis Dr. Charles Hufnagel paved the way for subsequent development of the wide variety of artificial valves in use today.

Developed the first successful heart-lung machine, to maintain heart and pulmonary function during open-heart surgery; the success of this and other pioneering advances stimulated development of many highly efficient machines employing a variety of new pumping and oxygenating principles.

Reported the first successful surgical repair of a ventricular aneurysm.

Developed the spectrophotofluorometer, an extremely sensitive instrument for identifying and quantifying biological substances.

Introduced a simple urinary test for malignant carcinoid. This tumor, often involving intestinal tissues, was virtually unknown before 1954, but as a result of the diagnostic test, was subsequently found to occur rather frequently.

Reported the first case in which the life of a human was saved by transplanting a kidney from another human at Peter Bent Brigham Hospital and Harvard Medical School in Boston.

Discovered the anti-hypertensive effectiveness of chlorothiazide. Chlorothiazide was found to be selective for hypertension, effective orally, and free of severe side effects. It was also found that chlorothiazide not only lowers blood pressure directly when used alone, but also greatly enhances the effectiveness of other anti-hypertensive agents when used in combination with them.

Challenged classic concepts of heart action in health and disease, and provided a valuable index of heart performance. It was found that the tension developed by the fibers of the heart muscle at each beat--not the amount of blood it pumps or the length of the muscle fibers--governs its demands on the coronary blood supply for oxygen.

Developed the transseptal method of inserting catheters into the left heart chambers. Because the method involves no external heart puncture, it avoids the risk of hemorrhage from the heart, lung damage, and air leakage that may attend other methods. Showed that microsomes located within cells of the liver are a principal means by which the body inactivates drugs. The microsomes contain enzyme systems that can change foreign compounds into forms which the kidney can excrete.

Developed the first practical technique of transplanting the heart--the one in widest use today. This technique leaves in place a portion of the recipient's right and left atria, simplifying and shortening the operation.

Introduced an entirely new approach to the production of concentrated antihemophilic globulin (AHG) used for treating hemophilia patients. It was shown that, using a standard double plastic bag set, any hospital or blood bank can easily make concentrates of AHG averaging 30 times the potency of frozen plasma, in such a way that the whole blood from which the concentrate was made can be "reconstituted" and banked for other uses.

Disclosed that persons with heterozygous as well as homozygous antitrypsin deficiency are subject to chronic obstructive lung disease at a relatively early age.

Reported the first clinical application of an electronic device that can halt or prevent the incapacitating chest pain of angina pectoris by electrical stimulation of the carotid sinus nerves.

Produced knowledge of the chemical structure, physiologic role and clinical potential of the calcium-regulating thyroid hormone, thyrocalcitonin. NIH studies defined the structural interrelationships of the 32 amino acids in the thyrocalcitonin molecule, and developed a sensitive method for assay of the hormone in the blood. They also provided the earliest demonstration of the therapeutic potential of this hormone in patients with hypercalcemic bone demineralization disorders.

Reported that electrophoretic analysis of blood lipoprotein patterns provides a simple, low-cost method of detecting and classifying blood lipid disorders that is superior to conventional determinations. By this method, they have been able to identify five distinct forms of genetically determined hyperlipoproteinemias.

Tested and evaluated new drugs for controlling hypertension, defining their modes of action, and recognizing their clinical potential; much of the pioneering work on enzyme inhibition as an approach to treatment was conducted by scientists who also were the first to establish the value of alpha-methyl DOPA.

Developed a red blood cell-freezing process which will preserve blood safely for several years.

Developed a highly promising artificial lung (spiral coil membrane blood oxygenator) which is undergoing preliminary tests of its ability to provide total respiratory support for newborn infants suffering from hyaline membrane disease and other forms of acute respiratory distress. Scientists recently incorporated this same oxygenator design into an experimental fetal support system (artificial placenta) that successfully maintained non-breathing fetal lambs for periods exceeding two days. Discovered that certain psychoactive drugs produce dramatic changes in brain amine concentrations, in addition to their pronounced behavioral effects. This prompted a great wave of investigation into the functions of amines as neurotransmitters and as possible mediators of mental disease.

"Cracked" the genetic code, an accomplishment which was later recognized by the award of the Nobel Prize for Physiology or Medicine.

Isolated the adenoviruses. Later, an effective live, oral vaccine was developed against adenovirus 4, the main cause of epidemics of severe acute respiratory disease in military training camps.

Isolated members of other virus families--the parainfluenzas and respiratory syncytial virus--and showed them to be the leading causes of serious respiratory illnesses in infants and young children.

Isolated <u>Histoplasma capsulatum</u>, the fungus responsible for the disease histoplasmosis. Evidence gathered over the years identified pigeon droppings as a similar important reservoir for the fungus causing the sometimes fatal disease, cryptococcosis.

Recovered, for the first time, the parasite, <u>Toxoplasma gondii</u>, from a human eye and demonstrated that some forms of eye disease can be caused by this organism. Later, the domestic cat was identified as a natural host in the life cycle of <u>T. gondii</u>, suggesting a possible relationship between cats and toxoplasmosis in humans.

Made important contributions in the field of transplantation immunology which have enhanced the likelihood that organs transplanted from one individual to another will "take".

Developed a quick and easy inhibition assay test with a few drops of blood for detection of PKU (Phenylketonuria), a genetic biochemical defect which causes mental retardation.

Developed in utero screening tests for detection of the specific enzyme causing Gaucher's, Niemann-Pick, and Tay-Sach's diseases, all of which can end in mental retardation and death. Screening tests have also been developed for detection of Wilson's disease, metachromatic leukodystrophy and several other abnormalities of amino acid metabolism.

Produced proof that subacute sclerosing panencephalitis (SSPE), a fatal brain disease of children, is caused by a measles virus which may reside in the body for many years after the acute infection.

Aided in development of surgical treatment (stapedectomy) for restoring hearing to more than 90 percent of patients with middle ear deafness (otosclerosis).

Developed a new tool, evoked response audiometry, for diagnosing hearing loss in babies and brain-damaged children, providing an early assessment of the degree of damage by presenting a true picture of the brain's response to sound. Developed the first simple and rapid test for detection of German measles (rubella). The complement-fixation blood test, which provides identification of antibodies to rubella infection within 24 hours, laid the ground work for the subsequent development of the Hemagglutination-Inhibition test currently being used.

Developed a brain scanner for detection of radioisotopes that is now widely used to diagnose and locate brain tumors. By following the flow of cerebrospinal fluid into which radio-iodinated human serum albumin has been injected, scientists can detect tumors, brain cysts, and derangements caused by injury, through modification in the brain scanning technique.

Identified three new forms of muscular dystrophy, and screening tests can now detect 65 percent of the carriers of progressive muscular dystrophy, the most common form.

Almost completely eliminated retrolental fibroplasia, once a major cause of blindness in premature babies, following clinical confirmation of the hypothesis that the disorder resulted from exposure to high levels of oxygen in incubators.

Found primary open-angle glaucoma, most common form of this potentially blinding disease, to be inherited as a recessive trait. Early identification and effective drug treatments for this and other forms of the disease have been developed which promise to reduce the incidence of blindness from glaucoma.

Advanced corneal transplantation, enabling sight to be restored and improved tests for assessing the vitality of donor material. In addition, special freezing techniques have been developed for preserving the cornea until needed. The use of immunosuppressive drugs has helped prevent rejection.

Developed techniques for the successful reattachment of retinal separations, including cryosurgery, photocoagulation by laser beams, diathermy, as well as alternate approaches such as refinements in scleral buckling.

Discovered a dramatic cure for herpes simplex keratitis, a common and hard-totreat viral infection which was a major cause of blineness due to corneal disease. The eye disease was successfully treated with the drug 5-iodo-2-deoxyuridine (IDU), originally developed for treating cancer. This was the first cure of a virus disease in man by drug therapy.

Developed fluorescein angiography, providing an important tool for the diagnosis of retinal disease which has helped in treating disorders of the macula, the area of the retina that permits the highest level of visual acuity.

Introduced antimetabolite therapy and improved X-ray therapy for treating retinoblastoma, a tumor of the eye in children, which has helped significantly to increase the survival of patients with this form of cancer.

Established a scientific base for water fluoridation as an effective cariespreventive procedure by demonstrating conclusively that the daily human intake of 1 part per million of fluoride ion reduces the incidence of dental caries (tooth decay) by 60 percent.

Contributed to an understanding of the mechanism by which the fluoride ion is incorporated in the developing tooth structure and acts to enhance its resistance to caries by changing the molecular structure of the crystal components of tooth enamel.

Added significantly to the essential body of knowledge that established dental caries as an infectious, transmissible disease, resulting from specific microorganisms.

Increased understanding of the mechanism by which bacterial plaque deposits operate in the causation of tooth decay, suggesting possibility of control through enzymatic, antibiotic, and antibacterial approaches.

Developed a better understanding of what are now believed to be multiple periodontal disorders, rather than a single disease entity. Evidence suggests that inflammation which leads to tissue damage in periodontal disease may be an allergic response to bacterial products. Scientists demonstrated that bacterial plaque formation plays a causative role in periodontal disease.

Discovered the existence of significant amounts of a connective tissuedestroying enzyme, collagenase, in gingival tissue under normal conditions, and strikingly increased amounts of this enzyme in patients with periodontal disease.

Developed important basic knowledge on the composition and structure of certain components of periodontal and other connective tissues, including (a) discovery of a previously unrecognized tissue fiber (oxytalan fiber), and (b) the finding that defects in the intramolecular and intermolecular crosslinking patterns in collagen may strongly influence the tissue breakdown which occurs in periodontal disease.

Developed new and improved diagnostic, surgical, and speech therapy techniques to enable cleft lip/palate victims to achieve near-normal appearance and function

Further clarified the interrelated roles of genetic and environmental factors in cleft palate etiology, and established experimentally that cleft palate is uniformly produced in the offspring when pregnant animals are exposed to certain stress situations or to certain drugs during critical stages of gestation.

Developed the new synthetic pain-killing drug, phenazocine.

Provided the first descriptions for a number of genetic defects, clarifying the basic error of metabolism in these and other birth disorders, such as galactosemia, Lesch-Nyhan Syndrome, and phenylketonuria. Initiated the technique of pre-birth, intra-uterine diagnosis of certain of these disorders, and developed methods of control, which in some cases prevent severe mental retardation and death. Supported research resulting in synthesis in the laboratory of important hormones such as ACTH, insulin, and, recently, a new hormone (thyrotropin-releasing) that is produced by the brain and governs one of the actions of the body's "master" gland, the pituitary.

Elucidated the causative mechanisms of gout and aided in providing highly effective treatment methods that make this painful disorder one of the most controllable and manageable of the arthritic diseases.

Developed improved methods of diagnosis and clinical management of cystic fibrosis.

Developed techniques of organ transplantation, primarily kidney transplantation. Transplantation now has become a major lifesaving treatment method for patients with end-stage kidney disease.

Discovered that the Pima Indians in Arizona have a rate of diabetes 15 times that of any population on record, as well as an extraordinarily high incidence of gallbladder disease.

Developed new and effective methods for the treatment and prevention of endemic goiter.

Demonstrated the efficacy of giving burn-shock patients large oral doses of salt and baking soda in water as an emergency treatment comparing favorably with administration of whole blood or plasma.

Demonstrated that the amino acid lysine, when added to wheat protein, can significantly improve growth of undernourished pre-school children. The NIHsponsored project was carried out in India.

Provided the first clue to the structure and function of the enzyme ribonuclease-an NIH scientist shared a Nobel prize in chemistry for this work.

Revealed that newborns exposed to long periods of artificial light do not develop hyperbilirubinemia, which causes jaundice that can lead to brain damage and retardation. The light treatment is particularly effective for premature babies.

Found that the lungs of infants who died from the respiratory distress syndrome attributed to hyaline membrane disease are deficient in surfactant. Surfactant, normally produced by the alveolar cells of the lungs, lubricates the surface of the lungs' air sacs and prevents their collapse.

Demonstrated in fetal sheep that when a fetus has insufficient oxygen the first pathological change occurs in the brain's electrical activity and is accompanied by a changed heart rate. Extensions of this study may lead to new ways of preventing brain damage and mental retardation. Reported success in using demineralized bone to trigger new bone formation--an achievement offering new hope for accident victims with shattered bones as well as for wearers of complete dentures.

Developed--under sponsorship of the Division of Biologics Standards--two monkey diploid cell lines which were approved by DBS for use in production of human viral vaccines. A human diploid cell line was approved for production of live poliovirus vaccine.

Discovered that some patients with abnormal heart rhythms can voluntarily learn to control these abnormalities and even maintain control after leaving the hospital, thereby improving health and activity.

Developed an electro-optical device, called the "Optisat," that provides continuous measurements of blood-oxygen levels during the use of heart-lung machines or respiratory assist devices.

Found RNA-dependent DNA polymerase, or reverse transcriptase, in more than 30 viruses known to cause cancer in animals, in human leukemia cells, and in some human milk specimens from women with family histories of cancer. The evidence suggests that the enzyme may be a key element in the change of normal cells to cancer cells.

Reported for the first time a practical animal model for serum hepatitis. An agent, presumably the virus of serum hepatitis, was successfully transmitted to rhesus monkeys. The virus stimulates the development of an antigen (HAA), often found in the blood of serum hepatitis patients and considered a marker for that form of the disease.

Reported advances in computer-based systems for drug surveillance. One new system prevents undesirable drug interactions in hospitalized patients by automatically monitoring all drugs dispensed to patients. It will ultimately produce a computer-generated "alert" each time a newly prescribed drug has the potential of interacting with a drug the patient is already receiving.

Reported detection of diabetes with a gingival biopsy. Diabetes involves both a metabolic defect and vascular pathology. When blood vessel involvement is severe, thickening of the basement membrane in the small blood vessels becomes more noticeable. Dentists treating periodontal disease could detect this thickening, allowing for early diagnosis of diabetes. A relatively painless procedure, gingival biopsy could provide microscopic evidence of early disease more readily than muscle biopsy.

Found the sexual forms of reproduction of <u>Histoplasma capsulatum</u>, the fungus that causes histoplasmosis. Observation of the mating between strains will give researchers a chance to conduct genetic studies and learn more about the disease-causing ability of the fungus.

Confirmed that the use of oral contraceptives is associated with impaired glucose tolerance, even though fasting glucose levels are normal. This finding suggests that a mild form of diabetes may occur in women taking "the pill."

Achieved the first synthesis of fully infectious virus deoxyribonucleic acid (DNA), an important preliminary to understanding virus duplication in cells.

Developed a tissue-matching test, employing mixed leukocyte cultures that led directly to the first successful bone marrow transplant between persons other than identical twins.

Developed a simple genetic test for an abnormality in the enzyme, pseudocholinesterase; the procedure reduces the risk for surgery patients with a genetic trait that prevents action of a drug commonly used to induce muscle relaxation under anesthesia.

Achieved--in collaboration with the AEC--a number of advances in analytic instrumentation, including the zonal ultracentrifuge for precise separation and collection of subcellular particles and viruses, and a centrifugal fast analyzer system which performs accurately and in a single operation clinical evaluations of blood and other body fluids for as many as 30 patients in as little as 30 seconds.

Introduced for use in clinical laboratory analyses a broad spectrum of standard reference materials--including organic as well as inorganic materials.

Developed the virus strain used in the first rubella vaccine licensed for use in this country.

Developed various life-saving devices, such as a "fetal intensive care unit" that allows sensitive monitoring of the fetus during labor and delivery. This unit, when used in combination with observations of the mother, permits researchers to identify subtle alterations in the physiological state of the fetus before gross changes become clinically evident.

Devised improved methods for identifying and reducing electrical hazards in surgical and patient care areas.

Elucidated the complete amino acid sequence of the first of six known protein components of lipoproteins, the transport molecules for most of the fatty substances (lipids) in human blood.

Found that diazepam, a tranquilizer and muscle relaxant, is an unusually safe and useful sedative for patients recovering from heart surgery. Unlike many tranquilizers, diazepam does not depress heart function and may even improve it. Successfully applied a newly-designed radio frequency respiratory technique that enabled an accident victim, paralyzed from the neck down, to resume activities as near normal as his disability would allow. Two miniature receivers, implanted in the subcutaneous tissue on the anterior chest wall, electrically stimulate the phrenic nerves upon receipt of impulses from a small pocket radio transmitter.

Developed a microwave exposure system with a well-defined, uniform field characteristic, permitting accurate quantitative studies of the effects of microwave radiation on biological systems at a precise frequency.

Designed a data management system to meet the needs of NIH researchers and managers, that allows file creation, updating, editing, maintenance and retrieval from a computer data base with very little programming on the part of the user. The users can also set up their own data-naming convention to control maintenance and retrieval functions related to the data base.

Supplied more than 100 investigators world-wide with nucleus inbred breeders for VRB rodent genetic repository pedigreed colonies, and provided the Frederick Cancer Research Center with inbred strains to assure the reliability of nucleus stock.

Identified asbestos as an important cause of lung disease and cancer among workers exposed to it.

Found the skeletal lead contained in city children's teeth to be five to ten times higher than that found in suburban children. Analysis with an atomic absorption spectrometer suggested that teeth shed by youngsters may provide a better means than blood samples for testing previous exposure to lead, and may also identify community areas with dangerously high levels of lead and other trace elements permanently stored in the skeleton.

Employed enzyme replacement therapy to temporarily enhance deficient enzyme levels in Fabry's disease in two patients--the first time that direct replacement of a missing enzyme yielded beneficient results in a genetic disorder.

Developed a sensitive new test for detection of antibody to <u>Mycoplasma</u> pneumoniae, an organism that causes outbreaks of acute respiratory infections seasonally. The test, a modification of a radioimmunoprecipitation procedure, should enable scientists to learn more about the disease pattern of this organism in man.

Successfully transplanted embryonic brain cells in young animals for the first time. The transplanted immature brain cells became functional and were not rejected by the host cells. While still in the basic research stage, these results are a highly encouraging step in understanding and correcting brain injury.

Developed a new finger-prick blood test that provides a simple, reliable, and rapid technique for mass analysis of lead poisoning in children.

Established an International Tumor Immunotherapy Register to serve as a center for the collection, storage and exchange of information on immunological methods of treating cancer. Physicians submit periodic progress reports and, in return, receive summaries of the most recent information.

Developed a new instrument for visualizing heart defects without the sometimes risky insertion of catheters and dyes into the bloodstream. The new 2-dimensional technique, called "echocardiography," is particularly valuable in diagnosing heart defects in the small hearts of infants and young children.

Pioneered a new, still experimental means of dissolving gallstones that may eliminate many high-risk gallbladder operations. Chenodeoxylic acid (chenic acid) therapy produced significant reductions in gallstone size, or their complete disappearance in more than half the patients studied.

Isolated a new biochemical entity--selenoprotein--that may prove useful in research on certain types of muscular dystrophy.

Developed a new nuclear scanning device which enables physicians to view and photograph a myocardial infarct. Where the scan shows an infarct, knowledge of its size and location permits more positive treatment, or dictate certain courses of treatment.

Cooperated with a pharmaceutical company in evaluating a new anticonvulsant drug (Tegretol), prior to its approval for prescription use by FDA. Tegretol is the first new anticonvulsant drug to be made available since 1960, and the first major advance in 20 years in the long-term treatment of grand mal and psychomotor epilepsy.

Developed a specialized cancer data base. Cancerline, as the system is called, contemplates the addition of 10,000 cancer chemotherapy abstracts annually, and will also include about 10,000 descriptions of current cancer research, including protocol summaries.



10 Center Drive Bethesda, MD 20892-1150 301-496-1080



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