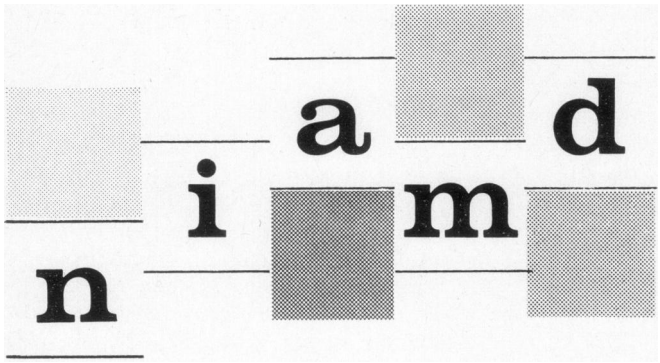
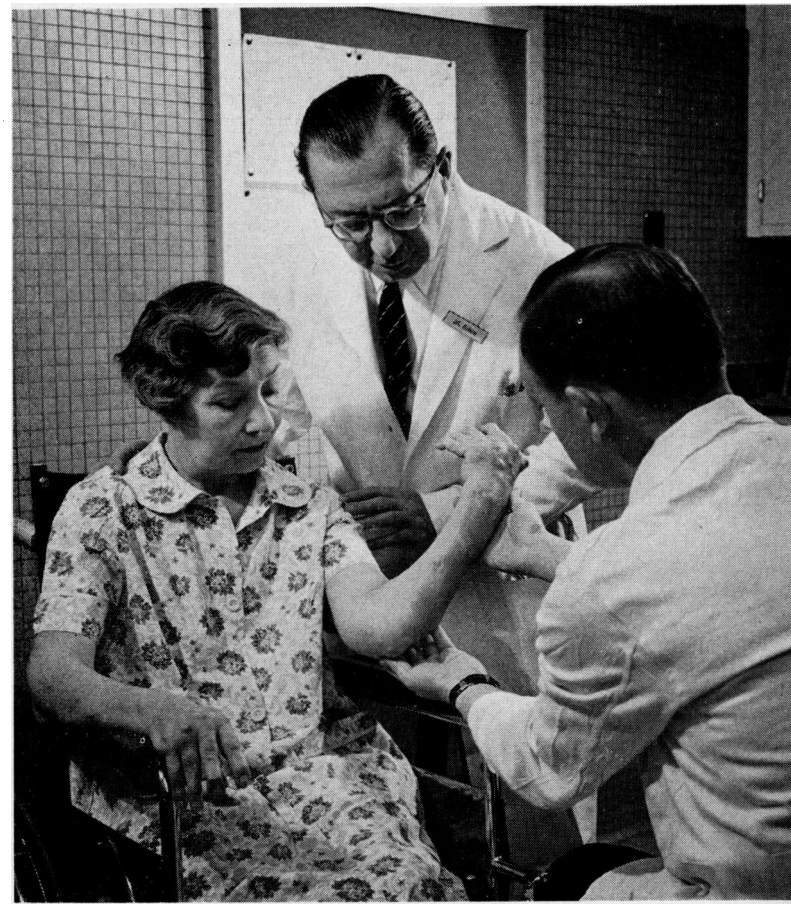


ten years

The National Institute of Arthritis and Metabolic Diseases of the Public Health Service recently celebrated its 10th anniversary with a public report to the Nation on research progress during the past decade. The institute was established in 1950 by the Omnibus Medical Research Act and resulted from a surge of interest in the arthritic disorders, spurred in large part by the discovery of cortisone. Although it was originally created for the study of arthritis and the then known metabolic disorders, the institute, located in Bethesda, Md., conducts and supports research in additional areas, including hematology, gastroenterology, cystic fibrosis, and in such basic disciplines as pharmacology, biochemistry, nutrition, and physical biology. The scientific accomplishments presented on the following pages indicate the wide scope of institute activities. They represent research conducted in the institute's own laboratories and by its grantee scientists throughout the country.

ADVANCE AGAINST ARTHRITIS



Dr. Joseph J. Bunim with arthritis patient

PREDNISONE, the first synthetic corticosteroid, was introduced into medicine by Dr. Joseph J. Bunim, clinical director of NIAMD, and his associates in 1954. This antiarthritic drug possesses important clinical advantages over the naturally occurring steroids, cortisone and hydrocortisone, because of a reduced tendency to cause retention of fluid when administered in conventional therapeutic doses. Prednisone and newer synthetic steroids, still under constant development, are largely replacing cortisone and hydrocortisone in the treatment of arthritis and allied disorders.

The cause of the connective tissue diseases remains unknown. But new work, stemming from the hypothesis of the Australian virologist Sir Macfarlane Burnet and research in the past decade, offers some possible clues. Burnet's theory concerns how disease results from an auto-immune process by which an individual develops antibodies against his own cells or tissues. Cells reproducing and mutating throughout life set up a constantly changing pattern of antibody-antigen formation which results in a never-ending problem of self-identification.

Two recent findings in the rheumatic diseases are significant although they do not prove the Burnet theory. The so-called rheumatoid factor, present in 85 percent of patients with rheumatoid arthritis, is a very large gamma globulin, possibly an antibody synthesized in plasma cells. It has been discovered that in systemic lupus erythematosus a whole series of antibodies is produced against many common nuclear constituents, particularly desoxyribonucleic acid, the genetic material. Researchers are testing to see if the facts of arthritis and lupus erythematosus support or clarify the Burnet hypothesis.

SYNTHETIC ACTH

THE SYNTHESIS OF ACTH may provide clues as to how this hormone teams up with cortisone to relieve arthritis. ACTH is produced by the pituitary gland, and its production stimulates the outer shell of the adrenal gland to release cortisone and other hormones into the system. Cortisone and cortisonelike drugs are used in the temporary remedial treatment of rheumatoid arthritis, rheumatic fever, and other diseases. But their specific action on these diseases is not yet known.

Until the synthesis was accomplished, only ACTH produced by animals or human beings was available for investigation and therapy.

Constructed in 1960 by biochemists at the University of Pittsburgh, the hormone has the biological activity of natural ACTH and represents the largest proteinlike molecule ever produced synthetically. Using many original devices, the NIAMD grantees constructed it by putting together 23 natural amino acids, the building blocks of proteins.

Researchers believe the new techniques can be used to modify the structure of ACTH to achieve medically important results. The synthesis may also pave the way for synthesizing even more complex proteinlike molecules and clarify the workings of the pituitary gland.

REMEDY FOR GALACTOSEMIA

THE BIOCHEMICAL cause of galactosemia, a rare but often fatal metabolic disorder in which children cannot utilize any form of milk in their diet, was discovered by Dr. Herman Kalckar and his associates at the institute in 1956. They found that galactosemic infants lacked a single enzyme in the blood needed to convert galactose to glucose, the sugar form used by the body for energy. This inherited enzyme deficiency results in the accumulation of an apparently toxic byproduct of galactose metabolism and accounts for the characteristic pattern of mental retardation, blindness, enlarged liver and spleen, and early death.

The biochemical discovery led to the development of a diagnostic test which has made it possible to diagnose the disease immediately after birth. This is essential, since the affected children will grow and develop normally on a milk-free diet. Continuing studies by other institute scientists have shown that injections of the female hormone, progesterone, enables galactosemic children to convert at least some galactose into glucose, and menthol has been found to have the same effect. These findings open the possibility that there may be ways to overcome this inherited defect and possibly others like it.

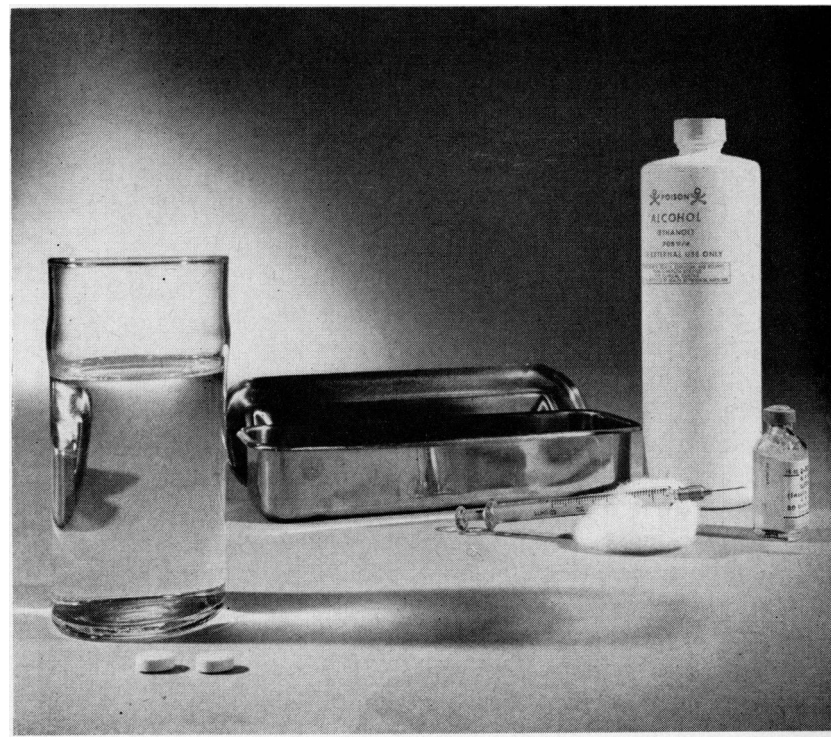
POWERFUL NEW PAINKILLER

DR. EVERETTE L. MAY, a chemist, and Dr. Nathan B. Eddy, a pharmacologist with NIAMD, have developed a potent new analgesic, phenazocine, which, is 5 to 10 times more powerful than morphine. The synthetic painkiller was derived from coal tar and has been clinically tested in thousands of patients. It relieves pain where optimal doses of morphine will not, and because of fewer and milder side effects it can be used for longer periods of time against chronic pain. Although it is a narcotic, phenazocine appears to be less addictive than the older drug; physical dependence develops more slowly and is less intense.

Phenazocine is one result of an intensive drug screening program at NIAMD which has evaluated nearly 8,000 compounds for their analgesic properties. Although not a final step, the new drugs represents significant progress toward the complete separation of the pain-relieving properties and the addiction potential of an analgesic drug.

Discovery of the synthetic drug also frees the United States from dependence on the foreign medicinal opium markets. Its developers have assigned all patent rights to the U.S. Government which has made them available to all countries.

PILLS REPLACE NEEDLES



ORAL ANTIDIABETIC drugs introduced in the last 10 years have replaced daily insulin injections in 500,000 patients, more than one-third of the Nation's diabetics. However, these drugs are not effective in a great number of diabetics, and they are not the oral insulin that has long been sought. Although these drugs are widely used, the way they lower the high levels of blood sugar is not fully understood.

The first of the new hypoglycemic drugs, tolbutamide, became available in 1957 after intensive trials by institute grantees and other physicians. Since then two others have been introduced, chlorpropamide and phenformin. The development of these drugs by the pharmaceutical industry has had a far greater impact than that of merely providing a more convenient form of treatment for selected patients. The extensive laboratory and clinical research which preceded the debut of tolbutamide sharply focused attention on fundamental problems in metabolism, endocrinology, and biochemistry, and stimulated a new wave of research on this ancient disease.

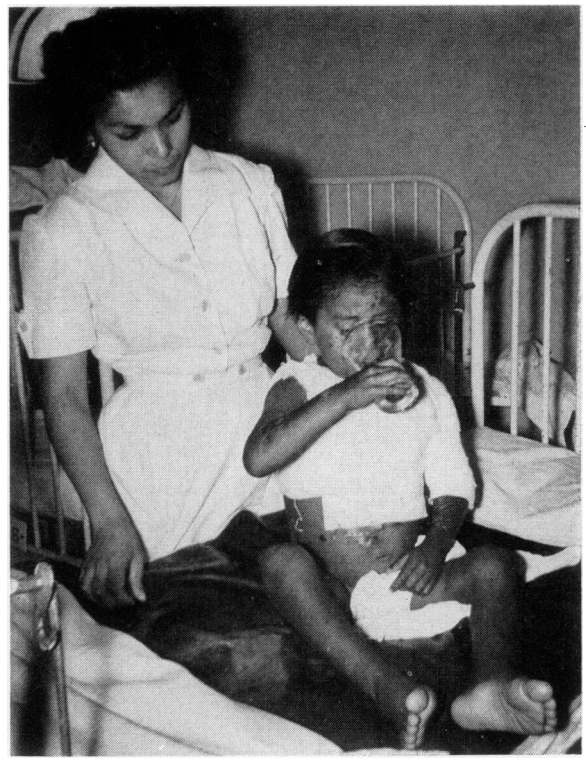
For example, the first large-scale study of the natural history of diabetes, scheduled to continue for a minimum of 10 years, began in 1960. Approximately 700 patients, 100 at each of seven research centers, will participate. The study is now in the pilot stage. The University Group Diabetes Study will investigate the incidence and severity of late complications such as retinopathy, atherosclerosis, neuropathy, and kidney disorders.

Within its own laboratories the institute is continuing laboratory and clinical investigations of diabetes. In one study substances antagonistic to insulin have been found in the plasma of patients with diabetes mellitus who have never received insulin therapy. This and similar studies of insulin's mode of action shed light on an important possible cause of diabetes other than pancreatic inability to produce insulin.

SALT AND SODA FOR BURN SHOCK

A KITCHEN REMEDY for the emergency treatment of shock due to burns—drinking a solution of 1 teaspoon of table salt and ½ teaspoon of baking soda mixed in a quart of tapwater—was developed by Dr. Sanford M. Rosenthal, Dr. Kehl Markley, Dr. Herbert Tabor, and Dr. R. C. Millican of the institute. The simple therapy would be of particular value in a major disaster or in isolated areas since neither skilled personnel nor bottles of blood are required. It is not designed to replace the traditional treatment of injections of whole blood, plasma, or the so-called plasma expanders.

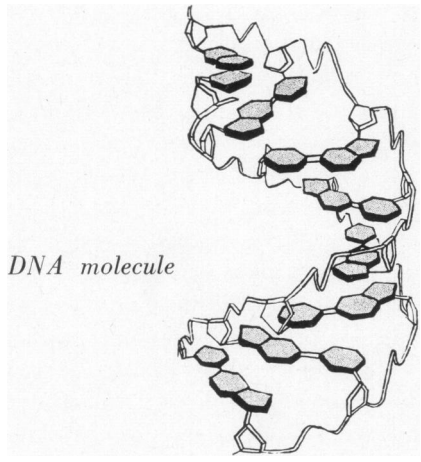
Burn shock, a semiconscious state marked by falling blood pressure and a lessening of the activities of vital body organs, accounts for a high proportion of the early deaths among victims of burns covering 10 percent or more of the body. From 1951 through 1959 the salt and soda solution therapy was evaluated clinically in burn shock victims in Peru. There were no deaths among adults. In infants, however, a combination of saline solution therapy with plasma was found to be more effective than saline solution alone or water and plasma alone.



Young Peruvian burn victim drinks salt and soda solution

CHEMISTRY OF HEREDITY

ONE OF THE ACHIEVEMENTS of basic research studies during the past 10 years was the biological synthesis of the genetic substances, DNA and RNA (desoxyribonucleic acid and ribonucleic acid). Dr. Arthur Kornberg, former chief of the institute's Laboratory of Biochemistry and Nutrition and now a grantee at Stanford University, succeeded in synthesizing DNA with the aid of a new enzyme which he discovered. Independently, Dr. Severo Ochoa, a grantee at New York University School of Medicine, discovered another enzyme which can synthesize RNA, and for their work the two scientists shared the 1959 Nobel Prize in Medicine.



DNA molecule

It is now generally believed that DNA carries the "code" that directs the synthesis of all proteins and the development of the cell, determining whether the cell becomes a brain cell or a liver cell. Like a tape recording, DNA carries specific instructions for the life processes of the cell. It is the master template of nature from which exact copies can be made so that the information it contains can be used elsewhere in time and space. The making of these copies is the function of RNA.