MEDICINE

New Cortisone Synthesis

➤ AN IMPROVED method of synthesizing cortisone, which promises to increase the supply of the now scarce arthritis remedy, was announced by Dr. E. C. Kendall and four Mayo Clinic co-workers at the meeting in Chicago of the American Chemical Society.

The nation's seven million or so arthritis sufferers probably never have heard of osmium. This is a very hard, gray metal which gets its name from the strong odor of one of its oxides. But the smelly hard metal in one of its forms, osmium tetroxide, has heretofore been necessary for the synthesis of cortisone.

Now Dr. Kendall and associates have found a way of making cortisone from bile acids without using osmium tetroxide.

"Cortisone may be made more cheaply and abundantly as a result," he declared.

Currently, he explained, "such large quantities of osmium are required and the supply is so limited that all pharmaceutical companies which would like to manufacture cortisone cannot secure the necessary amount of this rare element."

Osmium is not only expensive and rare but also toxic, so one part of the synthesis now followed required the recovery of all traces of osmium used in making cortisone.

Key to the preparation of cortisone is the introduction of what chemists call a hydroxyl group into the proper molecular position. It must be attached to the seventeenth carbon atom in a compound known as a pregnane derivative, which is extracted from cattle bile.

The new synthesis was accomplished by following precise chemical preparations of a series of intermediate compounds. The steps had to be delicately timed so that it was possible, through skillful manipulation, to remove the hydroxyl groups that entered the wrong positions, without removing the desired group. The success of this method is the culmination of four years of research work at the Mayo Foundation.

"The results could not be predicted," Dr. Kendall stated. "The achievement is a source of much satisfaction.

"The discovery of this series of intermediate compounds may be of no little significance in the large-scale production of cortisone. The sequence of steps can be applied to starting material other than that used in the work described in this paper and the ability to introduce a hydroxyl group at C-17 in derivatives of pregnane without the use of osmium tetroxide may remove a formidable block in the commercial production of cortisone."

Associated with Dr. Kendall in this work were Drs. Frank B. Colton, William R. Nes, David Van Dorp and Harold L. Mason.

Cortisone made without osmium has been produced in a radioactive form so that more can be learned about the path this drug takes through the body and, perhaps, how it acts to relieve arthritis and other ailments.

This feat was announced by Drs. T. F. Gallagher, Theodore H. Kritchevsky, David Fukushima, Bernard Koechlin and Max Eidinoff of Sloan-Kettering Institute and Memorial Hospital, New York.

Radioactive tritium was substituted for hydrogen in one stage of the synthesis to produce the radioactive cortisone.

Four other adrenal cortex hormones were also prepared and were made also with the stable isotope of hydrogen, deuterium, in the molecule. These hormones are also expected to aid in the study of the part these hormones play in fighting disease.

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NUCLEAR PHYSICS-GENETICS

Atom Alters Heredity

➤ DEFINITE proof that the atom bomb can alter plant heredity—and hence also the genetic legacy handed down by human atomic victims—has come from tiny seeds of cotton, barley and wheat brought back from Bikini.

Results of four years of experiments with seeds exposed to the atom bomb on the decks of the Bikini target fleet have been published in the JOURNAL OF HEREDITY (May) by scientists at Texas A. & M. College and the State College of Washington.

"From the standpoint of human welfare, proof that ionizing radiation released through the explosion of an atomic bomb can cause breaks in plant chromosomes means that human and animal chromosomes, as well as all others, are also liable to the same kind of injury," Dr. Meta S. Brown, Texas A. & M. specialist in genetics and the biology of individual cells, writes.

The Texas research showed that cotton grown from Bikini-radiated seeds had irregularities in the vital pairing of its chromosomes which could be attributed only to the atomic radiation.

From Pullman, Wash., Dr. Luther Smith reported similar changes in barley, wheat and oats. Both experiments were conducted as part of a long-term investigation by the Navy and the Agriculture Department into the biological effects of the A-bomb.

The cereals, Dr. Smith pointed out, had received the equivalent of 16,000 units of X-ray radiation, which is far more than a human being can take and still live.

Nevertheless, said the Texas report on cotton, "there is the possibility of hidden changes in chromosome structure which constitute a potential threat to the fertility of the individual (human being)."

"It has been repeatedly demonstrated that translocations and other structural changes in chromosomes have an adverse effect on the fertility of plants and animals," Dr. Brown reported.

Experiments such as these undoubtedly were the scientific backing for a warning on possible genetic changes published recently by the Atomic Energy Commission and Department of Defense in its handbook, THE EFFECTS OF ATOMIC WEAPONS.

"There is a large body of data which indicates that any dose of radiation, no matter how small, increases the probability of genetic changes," the AEC handbook said. To lessen the risk of passing on changes in chromosome structure, it advised atomic victims to "refrain from begetting offspring for a period of two or three months following exposure."

Science News Letter, September 16, 1950

MEDICINE

ACTH Saves Burned Man

➤ ONE of the wonder drugs relieving arthritis, ACTH, promises to become a lifesaver for badly burned soldiers and civilians who otherwise would die.

The American Chemical Society, discussing the chemical structure of this drug extracted from pituitary glands, heard of a case in Phoenix, Ariz., of a man badly third-degree-burned in an oil fire who was given ACTH with complete recovery after skin grafts. Without ACTH the man would have undoubtedly died, but the anti-arthritis drug prevented fluid loss, toxemia and muscle damage usual in such severe burns.

Armed service experts heard of the case, which was handled by Dr. Maurice J. Whitelaw, and observed it. As a consequence those handling ACTH production expect that it will be used medically at the fighting front. This may even slow down the application of the drug for treating arthritis and other diseases among civilians.

One of the newer uses of ACTH has been to combat acute alcoholism.

Dr. D. F. Waugh of the Massachusetts Institute of Technology reported to the chemists that the weight of the ACTH molecule was much smaller than previously supposed, between 1,000 and 1,300, that is, 1,000 to 1,300 times the weight of the hydrogen atom. This means that structure of ACTH is considerably simpler than